

REMARKS

Amendments to the Claims

Claims 1, 19, and 21 have been amended. Support for the Amendments to claims 1, 19 and 21 is found in the Specification at page 3, last paragraph. This Amendment incorporates the limitation of claim 26 into the independent claims. The amendment, therefore, does not raise a new issue after Final.

Claims 15 and 16 have been cancelled as dependent on a cancelled base claim. Claim 18 is herein cancelled.

No new matter has been added.

35 U.S.C. §103

1. Bosch

The Examiner rejects claims 1, 3-5, 9, 18, 19, and 21-26 under 35 U.S.C. §103 as unpatentable over Bosch (U.S. 2005/0059151)(hereinafter Bosch). Applicants respectfully traverse.

Applicants submit that one of skill would not have found the present invention obvious based on the disclosure of Bosch because Bosch does not disclose the explicit combination of LPS and IFN- γ , nor does Bosch provide data for any maturation period of less than 24 hours or any *in vivo* data.

The Examiner states that “[a]lthough Bosch does not teach the time range to expose the immature DCs to a combination of LPS and IFN γ , it would have been *prima facie* obvious to one of ordinary skill in the art” because “using the exposure time for the DC maturation protocol with LPS and IFN γ amounts to a simple substitution of one known, equivalent element for another to obtain predictable results.” (Office Action, page 5). The Examiner also states that the application of the 2-6 hour time point would have been routine optimization. Applicants respectfully disagree.

As discussed in the last response, the combination of LPS and IFN γ is not merely additive.

Bosch discloses that the priming of DCs with IFN- γ and BCG (bacille Calmette-Guerin) cause an increase in IL-12 production over either BCG alone or IFN- γ alone. (Bosch, Examples 1 and 3). Bosch suggests a 1-24 hour incubation time. (Bosch, ¶ [0040]). But, like Lapointe (cited in the Office Actions of September 16, 2008), Bosch only shows results *after* a 24 hour incubation. (Bosch, Example 1).

Bosch also teaches that:

Recently, enhancement of IL-12 production by dendritic cells has been reported by combining interferon gamma with certain dendritic cell maturation factors, such as bacterial lipopolysaccharide (LPS) and CD40. Both LPS and CD40 have a known capacity to induce small amounts of IL-12 during maturation, however. Thus, it is possible that the addition of IFN- γ merely enhances that production. . . . The mechanism for interferon gamma action in these cells has not been established. (Bosch, ¶ [0006]).

The Examiner fails to recognize that the Specification teaches that cells matured for 24 hours were injected as exhausted DCs. *See*, Specification, page 17. Thus, Bosch does not teach the critical difference between cells matured for 2-6 hours compared to cells matured for 24 hours.

Though the Examiner suggests that one of skill would have optimized the time point taught by Bosch, there is no reason to believe that one of skill would change both the maturation factor and the time point, when Bosch teaches that 24 hours is sufficient. Furthermore, the knowledge in the art at the time of filing is shown by Lapointe; which teaches that synergistic IL-12 production is *only* achieved at 24 or 48 hours. (Lapointe, Fig. 1C).

Lastly, Bosch does not provide any *in vivo* data. The present inventor discovered that IL-12 production ceases after a certain amount of time. For effectiveness of the present DCs a certain IL-12 production must be performed by the DCs within the body of the patient. Therefore, the 2-6 hour time point is used, to ensure that at least for some hours after administration of the activated DCs IL-12 production takes place within the patient.

Accordingly, Applicants submit that one of skill, reading Bosch, would have no reason to pick the combination of LPS and IFN γ or to choose a specific time point of 2-6 hours.

Furthermore, Applicants have presented evidence showing that the results obtained by using the specific method of exposure to LPS and IFN γ for 2-6 hours would be unexpected compared to using different maturation factors. As discussed in the last response, the Specification indicates that “active DCs” which produce IL-12 are therapeutically effective, whereas “exhausted DCs” which “do not produce IL-12 any more” are not effective in a tumor-specific manner *in vivo*. (Specification, page 4, lines 5-6; page 16, line 30, Figure 9).

Specifically, in mice given active DCs, 3/5, 4/5, or 5/5 mice were tumor free depending on whether they were given NPT from lysed cells, recombinant NPT, or NPT peptide fragments. (Figure 9). In contrast, only one mouse was tumor free in any of the mice treated with exhausted DCs. As Bosch only presents evidence of the application of exhausted DCs (that is, matured for 24 hours with different cytokines), one of skill would have no way to predict that the claimed method would be at least 3 times or 5 times as effective as the method Bosch actually suggests.

These results are supported by the evidence presented in the Felzmann (2005) paper (of record) and the Felzmann Declaration, showing effectiveness after a 6 hour maturation with LPS and IFN γ . Accordingly, Applicants submit that any *prima facie* case of obviousness is overcome in view of the evidence of unexpected results shown by the Specification and the Felzmann Declaration.

Applicants therefore request that the Examiner withdraw the obviousness rejection based on Bosch.

2. Bosch and Asavaroengchai

The Examiner also rejects claim 2 under 35 U.S.C. § 103 as unpatentable over Bosch in view of Asavaroengchai (of record). As discussed above, Applicants submit that teachings of Bosch do not render the presently claimed method obvious. Asavroengchai does not remedy any of the deficiencies Bosch with regard to either the maturation factors or the maturation time. Thus, one of skill would not have found the claimed method obvious. Accordingly, Applicants request that the Examiner withdraw the rejection of claim 2.

3. Bosch, Riser, and Felzmann (2000)

The Examiner rejects claims 6-8 under 35 U.S.C. § 103 as unpatentable over Bosch, Rieser (of record) and Felzmann (2000)(of record). As discussed above, Applicants submit that teachings of Bosch do not render the presently claimed method obvious. The addition of Rieser and Felzmann (2000) does not remedy any of the deficiencies Bosch with regard to either the maturation factors or the maturation time. Thus, one of skill would not have found the claimed method obvious. Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. § 112, second paragraph

The Examiner rejects claim 18 as lacking antecedent basis for "said active DC" in line 3. Claim 18 has been cancelled. Accordingly, Applicants request that the rejection be withdrawn.

Claim Objections

The Examiner objects to claim 18 as a substantial duplicate of claim 1. Claim 18 has been cancelled. Applicants request that the objection be withdrawn.

CONCLUSION

In view of the above remarks, Applicants request the Examiner withdraw all rejections.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Application No. 10/527,679
Amendment Dated July 17, 2009
In response to the Office Action Dated April 29, 2009

Docket No.: 4518-0110PUS1

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: July 17, 2009

Respectfully submitted,

By 

Leonard R. Svensson

Registration No.: 30,330

BIRCH, STEWART, KOLASCH & BIRCH, LLP

12770 High Bluff Drive

Suite 260

San Diego, California 92130

(858) 792-8855

Attorney for Applicant